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FILE 'HOME' ENTERED AT 14:26:42 ON 27 SEP 2005

=> file medline caplus embase biotechno biosis scisearch

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FILE 'BIOSIS' ENTERED AT 14:27:13 ON 27 SEP 2005

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FILE 'SCISEARCH' ENTERED AT 14:27:13 ON 27 SEP 2005
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=> s ixa
L1        5184 IXA

=> s fixa
L2         780 FIXA

=> s l1 or l2
L3        5649 L1 OR L2

=> s l3 and aptamer
L4          10 L3 AND APTAMER

=> s l3 and decoy
L5           0 L3 AND DECOY

=> dup rem l4
PROCESSING COMPLETED FOR L4
L6            8 DUP REM L4 (2 DUPLICATES REMOVED)

=> d ti 1-8

L6   ANSWER 1 OF 8  EMBASE  COPYRIGHT (c) 2005 Elsevier B.V. All rights
     reserved on STN                                    DUPLICATE 1
TI   The potential of aptamers as anticoagulants.

L6   ANSWER 2 OF 8  SCISEARCH  COPYRIGHT (c) 2005 The Thomson Corporation  on
     STN
TI   Aptamer to factor IXa and its matched antidote in
     cardiopulmonary bypass: An alternative to heparin and protamine

L6   ANSWER 3 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
TI   RNA in drug development

L6   ANSWER 4 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
TI   Therapeutic aptamers and antidotes: a novel approach to safer drug design

L6   ANSWER 5 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
TI   Modulators of pharmacological agents

L6   ANSWER 6 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
TI   RNA aptamers and methods for identifying the RNA aptamers specific for
     blood-coagulation factors, E2F transcription factor members and
     angiopoietins

L6   ANSWER 7 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN  DUPLICATE 2
TI   RNA aptamers as reversible antagonists of coagulation factor IXa

L6   ANSWER 8 OF 8  SCISEARCH  COPYRIGHT (c) 2005 The Thomson Corporation  on
     STN
TI   COAGULATION-FACTORS AND THEIR INHIBITORS


=> d 1-8 ab

L6   ANSWER 1 OF 8  EMBASE  COPYRIGHT (c) 2005 Elsevier B.V. All rights
     reserved on STN                                    DUPLICATE 1
AB   Useful additional options for anticoagulant therapy have been introduced
     over the last 15 years, including low-molecular-weight heparins and direct
     thrombin inhibitors. Despite these impressive advances, a need for safer
     effective anticoagulants remains. Aptamers represent a therapeutic
     modality that has the potential to address this unmet need. Aptamers are
     small nucleic acid molecules that function as direct protein inhibitors,
     much like monoclonal antibodies. Aptamers are delivered by parenteral
     administration, can be formulated to possess a very short or sustained
     half-life, and are purported to be nonimmunogenic. Perhaps most relevant
```

to the development of safer anticoagulant therapies, recent studies have shown that antidotes can be rationally designed to control the pharmacologic effects of aptamers in vivo, paving the way for a new class of antidote-controlled therapeutics. This review discusses the limitations of current anticoagulant therapies, the properties of aptamers and how these properties can be exploited to address the unmet needs within this therapeutic class, and the progress to date in developing new **aptamer**-based anticoagulant therapies. .COPYRGT. Published 2005, by Elsevier Inc.

L6 ANSWER 2 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AB A review on the principle and clin. application of RNA-based drugs and biosensors, discussing: (1) gene knockdown by using antisense oligonucleotides, ribozymes, dsRNA, siRNA, and group II intron, (2) RNA repair by trans-splicing using group I intron and spliceosome, (3) functional modification of proteins (VEGF, coagulation factor **IXa** , etc.) by RNA aptamers, and (4) RNA-based biosensors using allosteric ribozymes, aptazymes, and aptamers.

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AB A review describes the in vitro selection of aptamers using the SELEX process (systematic evolution of ligands by exponential enrichment). It illustrates that the anticoagulant activity of an **aptamer** targeting coagulation factor **IXa** can be rapidly and efficiently reversed by complementary oligonucleotides that can act as antidotes to the **aptamer**.

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AB The biol. activity of nucleic acid ligand is regulated (i.e. enhanced or inhibited) in vivo to produce a desired biol. effect. This is accomplished through the administration of a modulator, or regulator, that changes the binding of the nucleic acid ligand for its target or that degrades or otherwise cleaves, metabolizes or breaks down the nucleic acid ligand while the ligand is still exerting its effect. Modulators of the present invention can be administered in real time as needed based on various factors, including the progress of the patient, as well as the physician's discretion in how to achieve optimal therapy. Thus, this invention provides for the first time a regulatable therapeutic regime in the course of nucleic acid ligand therapy.

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AB RNA aptamers and methods for identifying the same are disclosed. The RNA aptamers selectively bind coagulation factors (factors **IXa**, thrombin, Xa, and VIIa), E2F family members (E2F-3), and angiopoietin-1 or angiopoietin-2. The pyrimidine residues of the RNA aptamers are modified to 2'-deoxy-2'-fluorocytidine and 2'-deoxy-2'-fluorouridine. The RNA aptamers are generated by SELEX (systematic evolution of ligands by exponential enrichment) or a modified toggle SELEX protocol. Blood-coagulation factor-specific aptamers display anticoagulant activity, and the angiopoietin aptamers prevent autophosphorylation of Tie2, an endothelial receptor tyrosine kinase activated by angiopoietin. Therapeutic and other uses for the RNA aptamers are also provided.

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
AB Many therapeutic agents are associated with adverse effects in patients. Anticoagulants can engender acute complications such as significant bleeding that increases patient morbidity and mortality. Antidote control provides the safest means to regulate drug action. For this reason, despite its known limitations and toxicities, heparin use remains high because it is the only anticoagulant that can be controlled by an antidote, the polypeptide protamine. To date, no generalizable strategy for developing drug-antidote pairs has been described. We investigated whether drug-antidote pairs could be rationally designed by taking advantage of properties inherent to nucleic acids to make antidote-controlled anticoagulant agents. Here we show that protein-binding oligonucleotides (aptamers) against coagulation factor

IXa are potent anticoagulants. We also show that oligonucleotides complementary to these aptamers can act as antidotes capable of efficiently reversing the activity of these new anticoagulants in plasma from healthy volunteers and from patients who cannot tolerate heparin. This generalizable strategy for rationally designing a drug-antidote pair thus opens up the way for developing safer regulatable therapeutics.

L6 ANSWER 8 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

AB A comprehensive three-dimensional picture of the coagulation process is beginning to emerge. Crystallographic structure determinations of prothrombin, factor Xa, factor **IXa**, tissue factor and factor XIII represent important advances in our understanding of the coagulation cascade. Similarly, structures of antithrombin, tissue factor pathway inhibitor and thrombomodulin provide details of endogenous anticoagulatory mechanisms. NMR spectroscopy of multiple domains of coagulation proteins represents an important contribution to the analysis of flexibility and rigidity of modular proteins. Thrombin, as the prime candidate for antithrombotic drug design, continues to be an object of intense efforts in applied crystallography.

=> d 1-8

L6 ANSWER 1 OF 8 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 1

AN 2005141131 EMBASE

TI The potential of aptamers as anticoagulants.

AU Nimjee S.M.; Rusconi C.P.; Harrington R.A.; Sullenger B.A.

CS B.A. Sullenger, Box 2601, DUMC, Durham, NC 27710, United States. b.sullenger@cgct.duke.edu

SO Trends in Cardiovascular Medicine, (2005) Vol. 15, No. 1, pp. 41-45. Refs: 28
ISSN: 1050-1738 CODEN: TCMDEQ

PUI S 1050-1738(05)00003-4

CY United States

DT Journal; General Review

FS 018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy

LA English

SL English

ED Entered STN: 20050414
Last Updated on STN: 20050414

L6 ANSWER 2 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2004:467933 SCISEARCH

GA The Genuine Article (R) Number: 818VN

TI **Aptamer** to factor **IXa** and its matched antidote in cardiopulmonary bypass: An alternative to heparin and protamine

AU Nimjee S M (Reprint); Keys J R; Pitoc G A; Quick G; Rusconi C P; Sullenger B A

CS Duke Univ, Med Ctr, Durham, NC USA

CYA USA

SO ARTERIOSCLEROSIS THROMBOSIS AND VASCULAR BIOLOGY, (MAY 2004) Vol. 24, No. 5, pp. E7-E7. MA 37.
ISSN: 1079-5642.

PB LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621 USA.

DT Conference; Journal

LA English

REC Reference Count: 0

ED Entered STN: 11 Jun 2004
Last Updated on STN: 11 Jun 2004

L6 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

AN 2003:232387 CAPLUS
DN 138:265004
TI RNA in drug development
AU Kozu, Tomoko
CS Saitama Cancer Cent. Res. Inst., Japan
SO Tanpakushitsu Kakusan Koso (2003), 48(4, 3Gatsugozoka), 540-548
CODEN: TAKKAJ; ISSN: 0039-9450
PB Kyoritsu Shuppan
DT Journal; General Review
LA Japanese

L6 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:664604 CAPLUS
DN 140:263303
TI Therapeutic aptamers and antidotes: a novel approach to safer drug design
AU Sullenger, B. A.; White, R. R.; Rusconi, C. P.
CS Department of Surgery, Duke University Medical Center, Durham, NC, 27710, USA
SO Ernst Schering Research Foundation Workshop (2003), 43(Human Gene Therapy: Current Opportunities and Future Trends), 217-223
CODEN: ESRWEL; ISSN: 0947-6075
PB Springer-Verlag
DT Journal; General Review
LA English
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:927447 CAPLUS
DN 138:19465
TI Modulators of pharmacological agents
IN Sullenger, Bruce A.; Rusconi, Christopher
PA Duke University, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002096926	A1	20021205	WO 2002-US16555	20020528
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2448567	AA	20021205	CA 2002-2448567	20020528
	US 2003083294	A1	20030501	US 2002-155233	20020528
	EP 1401853	A1	20040331	EP 2002-739409	20020528
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2005502596	T2	20050127	JP 2003-500105	20020528
PRAI	US 2001-293231P	P	20010525		
	US 2001-331037P	P	20011107		
	WO 2002-US16555	W	20020528		

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2002:256426 CAPLUS
DN 136:305828
TI RNA aptamers and methods for identifying the RNA aptamers specific for blood-coagulation factors, E2F transcription factor members and angiopoietins
IN Sullenger, Bruce A.; Rusconi, Christopher P.

PA Duke University, USA
SO PCT Int. Appl., 216 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002026932	A2	20020404	WO 2001-US30004	20010926
	WO 2002026932	A3	20020627		
	WO 2002026932	C2	20030320		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	CA 2425208	AA	20020404	CA 2001-2425208	20010926
	EP 1330544	A2	20030730	EP 2001-977167	20010926
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	US 2003175703	A1	20030918	US 2001-963827	20010926
PRAI	US 2000-235654P	P	20000926		
	WO 2001-US30004	W	20010926		

L6 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2
AN 2002:672267 CAPLUS
DN 138:297285
TI RNA aptamers as reversible antagonists of coagulation factor **IXa**
AU Rusconi, Christopher P.; Scardino, Elizabeth; Layzer, Juliana; Pitoc, George A.; Ortel, Thomas L.; Monroe, Dougald; Sullenger, Bruce A.
CS Program in Combinatorial Therapeutics, Department of Surgery, Duke University Medical Center, Durham, NC, 27710, USA
SO Nature (London, United Kingdom) (2002), 419(6902), 90-94
CODEN: NATUAS; ISSN: 0028-0836
PB Nature Publishing Group
DT Journal
LA English
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 8 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1995:59541 SCISEARCH
GA The Genuine Article (R) Number: QB630
TI COAGULATION-FACTORS AND THEIR INHIBITORS
AU STUBBS M T (Reprint); BODE W
CS MAX PLANCK INST BIOCHEM, D-82152 MARTINSRIED, GERMANY (Reprint)
CYA GERMANY
SO CURRENT OPINION IN STRUCTURAL BIOLOGY, (DEC 1994) Vol. 4, No. 6, pp. 823-832.
ISSN: 0959-440X.
PB CURRENT BIOLOGY LTD, 34-42 CLEVELAND STREET, LONDON, ENGLAND W1P 6LB.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 74
ED Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

WEST Search History

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☐	L8	l6 not l7	7
☐	L7	L5 and l4	7
☐	L6	L5 or l4	14
☐	L5	decoy and l3	10
☐	L4	aptamer and L3	11
☐	L3	l1 or L2	2551
☐	L2	fixa	130
☐	L1	IXa	2486

END OF SEARCH HISTORY